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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/643,411	08/19/2003	Kuo-Long Yu	CT-2645 DIV	3431

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EXAMINER	
ROBINSON, BINTA M	

ART UNIT	PAPER NUMBER
1625	

DATE MAILED: 04/23/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/643,411	YU ET AL.	
	Examiner	Art Unit	
	Binta M. Robinson	1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *1/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Detailed Action

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-10 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the compounds of formula I in claim 1 where R9 is pyrrolidine, R6 is thiazole, X is saturated pyrrole, tetrazole, piperidine, and 1, 2, 4-diazole, does not reasonably provide enablement for R9 equal to all heteroaryl rings one to two of the same or different heteroatoms selected from the group consisting of O, S, and N, R6 equal to all 5-membered heteroaryl rings containing one to two of the same or different heteroatoms selected from the group consisting of O, S, and N, X equal to all heteroaryl rings, 3-7 non-aromatic heterocyclic rings containing at least one and up to four non-carbon atoms selected from the group consisting of O, N and S. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

As stated in the MPEP 2164.01 (a), "There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue."

In *In re Wands*, 8 USPQ2d 1400 (1988), factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have need described. They are:

1. the nature of the invention,

2. the state of the prior art,
3. the predictability or lack thereof in the art,
4. the amount of direction or guidance present,
5. the presence or absence of working examples,
6. the breadth of the claims,
7. the quantity of experimentation needed, and
8. the level of the skill in the art.

The nature of the invention

The nature of the invention is the treatment of Respiratory syncytial virus with the compounds of formula I in claim 1, and the preparation of these compounds and their compositions.

The state of the prior art and the predictability or lack thereof in the art

The state of the prior art is that currently Ribavirin is only approved for the treatment of Respiratory syncytial virus. Yu et. al. (WO 0200004900) (See Reference N) discloses a series of substituted benzimidazoles that are substituted with benzotriazoles as useful in the treatment and prevention of RSV infection. A related series of compounds were first disclosed by F. Pagani and F. Sparatore in Boll Chim Farm. 1965, 104, 427 (See Reference V) and G. Paglietti et. al. in Il Farmaco, Ed. Sci. 1975, 30, 505 (See Reference W) and were found to possess analgesic and antiarrhythmic activity. CA 92:128844 is cited to show the state of the prior art. CA 92:128844 teaches benzimidazole I compounds where the Q moiety is a quinazolinone. Therefore, no predictability of the chemical structure of the instant claims relating to antiviral activity can be concluded.

The amount of direction or guidance present and the presence or absence of working examples

The only direction provided in the specification are examples that were synthetically prepared where the compounds of formula I have R9 equal to pyrrolidine, R6 is thiazole, X is saturated pyrrole, tetrazole, piperidine, and 1, 2, 4-diazole. An assay testing the claimed compounds' antiviral activity against Respiratory syncytial virus was disclosed in the specification. However, the specification does not disclose any data regarding these compounds in their antiviral activity against Respiratory syncytial virus. So the specification lacks sufficient amount of direction and guidance presented regarding the antiviral activity of these compounds on Respiratory syncytial virus is low.

The breadth of the claims

The breadth of the claims is the treatment of Respiratory syncytial virus with the claimed compounds, which encompassed enormous, diverse chemical structures independent and distinct from each other.

The quantity of experimentation needed

The quantity of experimentation needed would be undue when faced with the lack of direction and guidance present in the instant specification in regards to the treatment of Respiratory syncytial virus with the claimed compounds, and the highly unpredictable nature of the field.

The level of the skill in the art

Based on the unpredictable nature of the invention and state of the prior art and the extreme breadth of the claims and lack of guidance and direction for for the treatment of RSV with the claimed compounds, one skilled in the art could not use the claimed invention without undue experimentation.

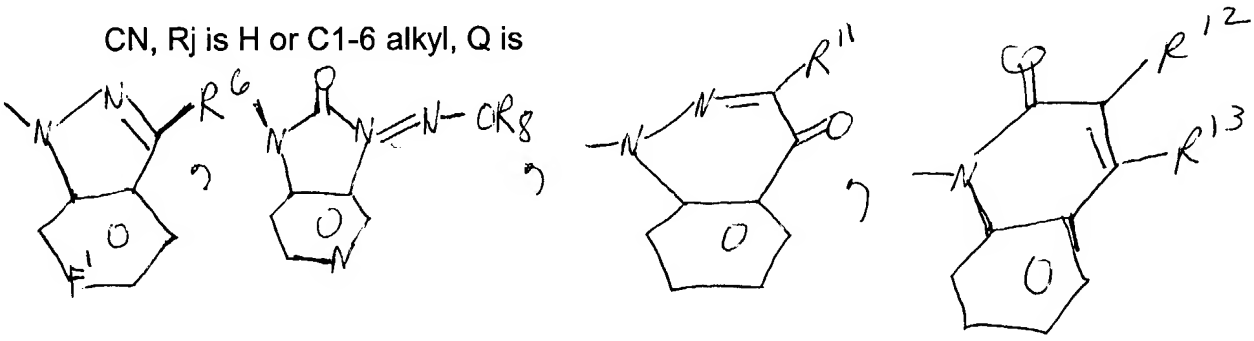
2. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claim 1 is provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 1 of copending Application No. US 20030207868. Although the conflicting claims are not identical, they are not patentably distinct from each other because the US 20030207868 patent application (See Reference U) is claiming antiviral,2-methylbenzimidazole derivatives that are used to treat RSV that only differ from the anti-RSV instant compounds in the R5 moiety. US 20030207868 patent application et. al. teaches the compound as shown in Formula I, where R1 is –(CraRb)n-X, Ra and Rb are each independently selected from the group consisting of H and C1-6 alkyl; said C1-6 alkyl being optionally substituted with one to six same or different halogen, X equal to H or C1-6 alkyl, said C1-6 alkyl being optionally substituted with halogen, Orc or S(O)mRd, Rc is H, Rd is C1-6 alkyl, n is 1-6, m is 0-2, R2 is H, R3 is C1-6 alkyl, R4 is C1-6 alkyl, said C alkyl optionally substituted with a member selected from the group consisting of halogen, R5 is selected from

CO2Rj, C1-6 alkyl optionally substituted with CN, Orc or NRfRg and C2-6 alkenyl with CN, Rj is H or C1-6 alkyl, Q is



, R2 is CH or N, R6 is H, halogen, C1-6 alkyl or C2-6 alkenyl, R8 is H or C1-6 alkyl, said C1-6 alkyl optionally substituted with one to three halogens, R9 is C1-6 alkyl or C3-6 cycloalkyl, said C1-6 alkyl optionally substituted with one to three halogen, R10 is C1-6 alkyl or C3-6 cycloalkyl, said C1-6 alkyl optionally substituted with one to three halogen, R11 is H or C1-2 alkyl, R12 is H, R13 is H. At column 64 and 65, see the compound of formula I where the radicals are as defined. The difference between the prior art compound and the instantly claimed compounds is the teaching of a subgenus of compounds in the US 20030207868 patent application where R5 is the only moiety that differs between the US 20030207868 patent application compound and the instant compound. In the instant compound, R5 must be halogen or H, whereas in the US 20030207868 patent application compound, the R5 must be selected from CO2Rj, C1-6 alkyl optionally substituted with CN, Orc or NRfRg and C2-6 alkenyl with CN, Rj is H or C1-6 alkyl. The instant compound and the US 20030207868 patent application compound are structurally the same except for the R5 moiety and also are used to treat RSV. Therefore, it would have been obvious to one of ordinary skill in the art to select

various known radicals within a genus to prepare structurally similar compounds that treat RSV. Accordingly, the compounds are deemed unpatentable therefrom in the absence of a showing of unexpected results for the claimed compounds over those of the US 20030207868 patent application art compounds.

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

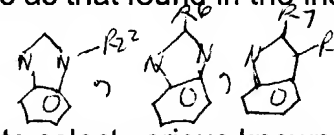
A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-10 respectively provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-10 respectively of copending Application No. 09994012 (US Patent Application Publication 2002/0099208). Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant application is claiming a subgenus of the 09994012 compounds, pharmaceutical compositions containing these compounds, and a method of treating mammals infected with RSV, with these compounds.

The difference between the prior art compounds, pharmaceutical compositions, and a method of treating RSV is that the applicant is claiming a subgenus and the

instantly claimed compound is that subgenus of the 09994012 compounds, pharmaceutical compositions containing these compounds, and a method of treating mammals infected with RSV, with these compounds.

(US Patent Application Publication 2002/0099208) teaches the genus of compounds of formula I, pharmaceutical compositions containing compounds of formula I, and a method of treating RSV with compounds of formula I that are of the same formula as the instant compounds and have all of the same radicals as that found in the instant compounds, except that Q can be three extra rings:  . It would have been obvious to one of ordinary skill in the art to select various known radicals within a genus to prepare structurally similar compounds. For instance, see the compound 193, at column 81, where a disclosed species is exemplified. Accordingly, the compounds, pharmaceutical compositions containing the instant compounds and a method of treating RSV with the instant compounds are deemed unpatentable therefrom in the absence of a showing of unexpected results for the claimed compounds over those of the generic prior art compounds.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double

patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claim 1 is rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 2, 4, 5 of U.S. Patent No. 6489338 in view of US Patent Application 2003/020868. Although the conflicting claims are not identical, they are not patentably distinct from each other because 6489338 is claiming of Q as a 2-oxo-imidazo [4,5-c]pyridin-3-yl ring whereas the instant application is claiming Q equal to the ring, 1H-pyrrolo[2,3-c]pyridine-2,3-dione oxime.

US 6489338 teaches the instant compound as shown in Formula I, where W is S, O, R1 is –(CR'R')n-X, X is H, C1-6 alkyl, said alkyl being optionally substituted with one to six of the same or different halogen atoms; n is 2-6, R2 is H, C1-12 alkyl, R3, R4, R5 and R6 are hydrogen, halogen, A, B, D, are C-H, E is N, R', R' are H, C1-6 alkyl, the alkyl being optionally substituted with one to six of the same or different halogen atoms. At column 139, see the compound of formula I and the radicals defined. The difference between the prior art compound and the instantly claimed compounds is the teaching of Q equal to a 2-oxo-imidazo [4,5-c]pyridin-3-yl ring whereas the instant application is claiming Q equal to the ring, 1H-pyrrolo[2,3-c]pyridine-2,3-dione oxime. US Patent Application 2003/020868, teaches the compound of formula I where Q can equal 2-oxo-imidazo [4,5-c]pyridin-3-yl ring or 1H-pyrrolo[2,3-c]pyridine-2,3-dione oxime and therefore, that 2-oxo-imidazo [4,5-c]pyridin-3-yl ring is an obvious variant of 1H-pyrrolo[2,3-c]pyridine-2,3-dione oxime. In view of US Patent Application 2003/020868,

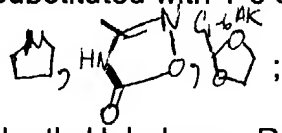
it would have been obvious to one of ordinary skill in modify the Q moiety of the 6489338 compound, to an obvious variant. Accordingly, the compounds are deemed unpatentable therefrom in the absence of a showing of unexpected results for the claimed compounds over those of the generic prior art compounds.

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 9, 10 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 2, 9 and 10 respectively of U.S. Patent No. 6506738 in view of US patent application, US 2003/0207868. Although the conflicting claims are not identical, they are not patentably distinct from each other because 6506738 discloses a genus of compounds where Q is 2-oxo-1-H-benzimidazole-1-yl instead of the instantly claimed 2-thioxo-1-H benzimidiazole-1-yl, a pharmaceutical composition comprising said compounds, and a method for treating mammals infected with RSV with said compounds, which are obvious variants of the instant claims.

US 6506738 patent teaches the instant compound as shown in Formula I where R1 is –(CRvRw)n-X; Rv and Rw are independently selected from the group consisting of H, C1-6 alkyl, said C1-6 alkyl being optionally substituted with 1-6 of the same or different halogen or hydroxy, or X being the rings  ;R2 is C1-6 alkyl, R3, R6 are each independently H, R5 is independently H, halogen, R11 and R12 are each independently H. At columns 204-205, see the compound of formula I, where the radicals are defined. The difference between the prior art compounds, pharmaceutical compositions containing said compounds and the method treating RSV with the said compounds and the instantly claimed compounds, pharmaceutical compositions and method of treating RSV with the said compounds is the teaching of compounds, pharmaceutical compositions containing said compounds and a method of treating RSV with said compounds, where Q is 2-oxo-1-H-benzimidazole-1-yl instead of the instantly claimed 2-thioxo-1-H benzimidiazole-1-yl. US Patent Application 2003/020868, teaches the compound of formula I where Q can equal 2-oxo-imidazo [4,5-c]pyridin-3-yl ring or 1H-pyrrolo[2,3-c]pyridine-2,3-dione oxime and therefore, that 2-oxo-imidazo [4,5-c]pyridin-3-yl ring is an obvious variant of 1H-pyrrolo[2,3-c]pyridine-2,3-dione oxime. In view of US Patent Application 2003/020868, it would have been obvious to one of ordinary skill in modify the Q moiety of the 6489338 compound, to an obvious variant. and a pharmaceutical composition containing said compounds, as well as a method of treating RSV with said compounds. Accordingly, the compounds, pharmaceutical compositions and method of treating RSV are deemed unpatentable therefrom in the absence of a showing of unexpected results for the claimed compounds,

pharmaceutical compositions and a method of treating RSV over those of the US 6506738 compounds, pharmaceutical compositions, and a method of treating RSV with said compounds.

The IDS filed 1/12/04 has been considered. The references that have been crossed out will not be considered until provided to the examiner.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Binta M. Robinson whose telephone number is (703) 306-5437. The examiner can normally be reached on M-F (9:30-6:00).
If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Mr. Joseph McKane, can be reached at (703) 308-4537.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone numbers are (703) 308-1235 and (703) 308-0196.

A facsimile center has been established. The hours of operation are Monday through Friday, 8:45AM to 4:45PM. The telecopier numbers for accessing the facsimile machine are (703) 308-4242, (703) 305-3592, and (703) 305-3014.

BMR

CEILA CHANG
PRIMARY EXAMINER
GROUP 1200 1625